REMARKS

Applicants have amended Claims 18-20 to exclude embodiments in which R^6 could represent -$CONR^8R^9$ in which either R^8 or R^9 could be hydrogen, as well as to correct minor typographical errors having no effect on the scope of the claims. The definition of R^6 retains the subject matter of allowable Claims 26 and 28.

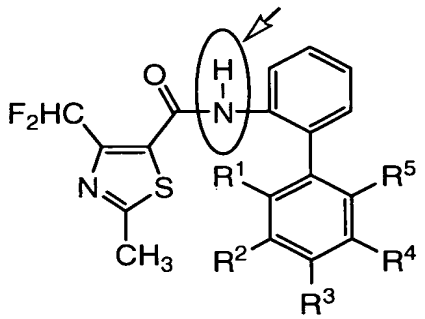
Allowable Subject Matter

Claims 26 and 28 stand objected to as being dependent upon a rejected base Claim 18. Applicants gratefully acknowledge the indication that these claims would be allowable if written in proper independent form. In view of the amendment of Claim 18 as discussed below, Applicants have not amended Claims 26 and 28 as kindly suggested by the Examiner but instead submit that they are allowable as written.

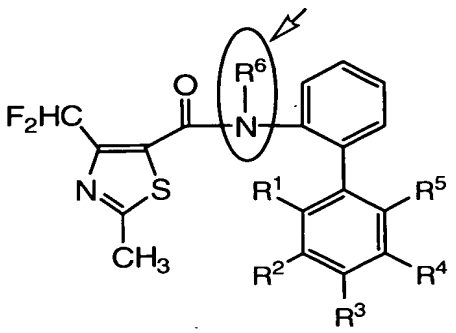
Double Patenting Rejection

Claims 18-25, 29, and 31-33 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 22-33 and 35-37 of copending Application No. 10/502,994. Applicants respectfully traverse.

The '994 application is directed to carboxamides of the formula



in which $\mathbf{R^1}$, $\mathbf{R^2}$, $\mathbf{R^3}$, $\mathbf{R^4}$, and $\mathbf{R^5}$ are independently hydrogen, halogen, cyano, nitro, (halo)alkyl, alkenyl, (halo)alkoxy, (halo)alkylthio, (halo)alkylsulfonyl, or cycloalkyl, or R^1 and R^2 together or R^2 and R^3 together can be optionally substituted alkylene. E.g., page 1, lines 11-24. The '994 application, however, discloses only an unsubstituted amide group (as shown by the oval and arrow above), whereas Applicants' claims specify compounds in which the bridging amide group must be N-substituted as shown below in formula (I) by the oval and arrow



(I) .

Although the Office Action at page 4 asserts that such substitution would be obvious to those skilled in the art, the Office Action provides no objective evidence that those skilled in the art would be led to make such compounds or that any such compounds would exhibit the activities found by Applicants. (For example, if the amide group is involved in an interaction with a biological receptor, modification of the group might be expected to affect such interaction in an unpredictable way.) Certainly, nothing in '994 application itself suggests N-substitution. Applicants note in this regard that the nitrogen atom at issue is an amide nitrogen, not an amine nitrogen as stated in the Office Action. What one might surmise about the relationship of one amine to another is believed not relevant to amides.

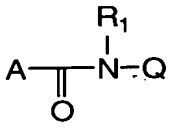
Furthermore, as will be discussed in more detail below, Applicants enclose a Declaration under 37 C.F.R. 1.132 of Dr. Ulrike Wachendorff-Neumann showing enhanced activity for a compound in which the bridging amide nitrogen atom is N-substituted according to Applicants' invention compared to a corresponding unsubstituted compound of the '994 application.

Applicants therefore respectfully submit that their claimed invention is patentably distinct from the '994 application and thus do not at this time offer a terminal disclaimer.

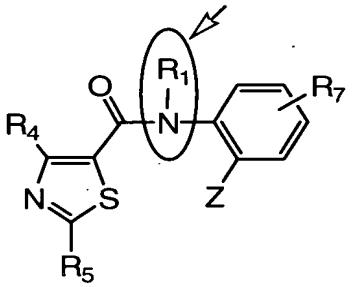
Rejection under 35 U.S.C. 103

Claims 18-25, 27, and 29-33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/059086 ("Walter et al") and CA 2,474,902 ("Elbe et al"), each taken alone or in combination with each other and each in further combination with JP 08/176112 ("Kanji et al"). Applicants note that Elbe et al is a Canadian counterpart of the '994 application discussed above with respect to double patenting and that that Walter et al is a counterpart of published US 2004/0138265. Applicants respectfully traverse.

Walter et al discloses microbicidal carboxamides having the general formula

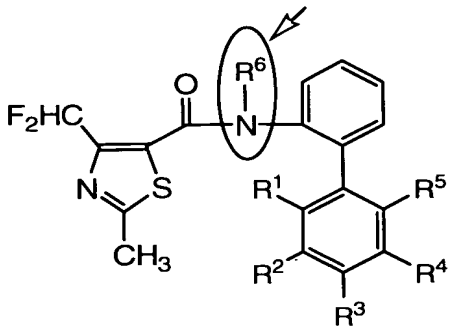


in which A represents several heterocycles, Q represents several aromatic groups, and R_1 represents an unsaturated hydrocarbon group having at least one carbon-carbon multiple bond or a carbonyl group. E.g., pages 1-2. Included within this large array of possibilities are compounds that can be represented by the following formula in which A is group (A3) and Q is group (Q1) of the reference:



wherein **R_1** is CH–C≡C-R_2, $CH_2CH=CHR_2$, $CH=C=CHR_2$, or COR_3; **R_2** is hydrogen or one of several carbon-containing substituents; **R_3** is optionally substituted C_1-C_6alkyl (in which the optional substituent is halogen, C_1-C_6alkoxy, or C_1-C_6haloalkoxy) or is C_1-C_6alkylthio, C_1-C_6haloalkylthio, C_1-C_6alkoxy, C_1-C_6haloalkoxy, C_3-C_6alkenyloxy, C_3-C_6haloalkenyloxy, C_3-C_6alkynyloxy, or C_3-C_6haloalkynyloxy; **R_4** is methyl that is optionally fluorinated (including, among others, CF_2H) or is chlorine or bromine; **R_5** is methyl or one of three other narrowly defined groups; and **Z** is phenyl or halophenyl, optionally substituted C_5-C_7 cycloalkyl, or a branched alkyl group. E.g., page 1, second paragraph, continuing over to page 2. That is, Walter et al discloses compounds in which the bridging amide group (shown by the oval and arrow above) is substituted with either an unsaturated hydrocarbon group having at least one carbon-carbon multiple bond or a carbonyl group (i.e., COR_3) connected to a narrowly defined set of optionally substituted alkyl, alkoxy, alkylthio, alkenyloxy, or alkynyloxy groups (i.e., R_3).

In contrast, Applicants' claims are directed to thiazolylbiphenylamides of formula (I)



(I)

in which the bridging amide nitrogen atom (as again shown by the oval and arrow above) is substituted either by non-carbonyl R^6 groups that are entirely different from the unsaturated hydrocarbon groups taught by Walter et al or by certain carbonyl-containing R^6 groups.

Applicants first submit that the compounds of their invention in which the amide substituent is not a carbonyl group are clearly not taught or suggested by Walter et al.

Applicants also submit that compounds of their invention in which the amide substituent is attached to a carbonyl group are also patentable over Walter et al. Applicants are aware that their group R^6 can include carbonyl groups similar to the carbonyl group COR_3 of the reference. In particular, among the many meanings of R_1 of the reference can be found a carbonyl group COR_3 in which R_3 is an optionally substituted alkyl group or an alkoxy or haloalkoxy group. At first glance, this might seem suggestive of compounds of Applicants' invention in which R^6 represents $-COR^7$ in which R^7 is an alkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkoxy, or halo-alkoxyalkyl group. However, this aspect of Walter et al must be viewed in proper context. To arrive at compounds of this type, one would need to select one of the five heterocyclic structures of group A (i.e., specifically thiazoles (A3)), no more than two of the ring structures of group Q (i.e., specifically substituted phenyl group (Q1) and perhaps group (Q6)), one of the several groups specified for group R_4 (i.e., specifically CF_2H), and one of the several groups specified for group R_1 (i.e., COR_3, and even then only for some of the substituents R_3). Nowhere does Walter et al teach the particular combination of structural features that characterize Applicants' claimed invention. Moreover, the reference does not show even one specific

example of a compound in which A is a thiazole and R_4 is a group other than CF_3. See list at page 11, as well as entries 4.01 through 4.46 in the table at pages 31-33. [It may be noted that the only specific compounds for which R_4 is CF_2H are a few pyrazoles of type (A1) listed at page 10 and in the table at pages 23-27, all of which are outside the scope of Applicants' claims.] For this reason alone, Applicants submit that their claimed invention is distinguishable from Walter et al. It may be noted in this respect that the indicated allowability of Applicants' Claim 26 (where R^7 is hydrogen and R^6 is thus a formyl group) and Claim 28 (where R^7 is 4-(difluoro-methyl)-2-methyl-1,3-thiazol-2-yl) is consistent with Applicants' belief that all embodiments of their invention as claimed should be allowable.

In further support of their position that their claimed invention is patentably distinct from Walter et al, Applicants refer to the enclosed Declaration under 37 C.F.R. 1.132 of Dr. Ulrike Wachendorff-Neumann (mentioned above with respect to the double patenting rejection), which provides data in Example Set I showing that a compound in which the thiazole moiety bears a difluoromethyl substituent according to Applicants' invention exhibits significantly enhanced activity compared to a thiazole compound of Walter et al that differs only in having a trifluoromethyl substituent (see Ex. 4.32 at page 33 of the reference).

Applicants therefore submit that their claimed invention is not rendered obvious by Walter et al.

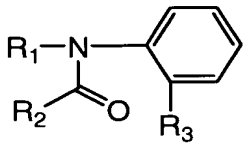
As discussed above with respect to the obviousness-type double patenting rejection, **Elbe et al** discloses carboxamides in which the bridging amide nitrogen atom is not N-substituted, whereas the compounds of Applicants' invention must be N-substituted. For essentially the reasons discussed with respect to the double-patenting rejection, Applicants submit that Elbe et al would not itself lead those skilled in the art to their claimed invention. Applicants further submit that Elbe et al, even when taken with Walter et al, would not lead those skilled in the art any closer to their claimed invention than what is disclosed in Walters et al.

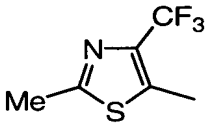
The Declaration of Dr. Wachendorff-Neumann also provides support for Applicants' position with respect to Elbe et al. In addition to providing the data mentioned above with respect to difluoromethyl substitution, the Declaration presents data in Example Sets II, III, and IV showing that the same thiazole compound of Applicants' invention used in Example Set I (which it must be noted for

the purposes of this discussion has an N-substituted bridging amide nitrogen atom) exhibits significantly enhanced activity when compared to a corresponding compound of Elbe et al in which the amide nitrogen atom is not substituted (see Ex. 21 of Elbe et al).

Applicants therefore submit that their claimed invention is patentably distinct from Elbe et al.

Kanji et al discloses carboxamides of the formula



in which $\mathbf{R_1}$ can be any number of groups, including acyl groups of formulas -CO-R_4 (where R_4 can be alkyl, haloalkyl, or phenoxymethyl) or a second amide moiety -CO-NH-R_5 (where R_5 can be alkyl or phenyl), as well as certain ethers R_6 or alkyl groups R_7; $\mathbf{R_2}$ can be a variety of cyclic groups, including a specific trifluoromethyl-substituted thiazole moiety having the formula  ; and $\mathbf{R_3}$ can be any of a variety of cyclic or unsaturated groups, including phenyl. E.g., pages 1-2 (as well as *Patent Abstracts of Japan*). Kanji et al, however, does not teach or suggest thiazoles having any other substitution pattern and does not teach or suggest a difluoromethyl substituent such as required by Applicants.

Moreover, Kanji et al does not disclose compounds in which the amide nitrogen atom is substituted with a formyl group (i.e., where R_4 of the reference could be hydrogen) or any other acyl groups specified by Applicants. Applicants note with respect to the second amide moiety -CO-NH-R_5 taught by Kanjii et al that the second amide group always has one hydrogen atom and one alkyl or phenyl substituent. For embodiments of Applicants' claimed compounds in which R^6 can be a second amide substituent -CONR^{8}R^9, neither R^8 nor R^9 can be hydrogen. Therefore, even if Kanji et al could be read to suggest the interchangeability of the groups it discloses as asserted in the Office Action, Applicants submit that Kanji et al would not lead those skilled in the art to the particular embodiments they claim.

As already discussed above, the Declaration of Dr. Wachendorff-Neumann shows the significance of difluoromethyl substitution in the thiazole moiety according

to their invention relative to trifluoromethyl substitution and thus further supports Applicants' position that Kanjii et al would not lead those skilled in the art to their claimed invention.

Applicants therefore respectfully submit that their claimed invention is not rendered obvious by Walter et al and Elbe et al, whether taken alone or in combination with each other or in further combination with Kanji et al.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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